Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

The March 15, 2005, interview between Examiner Ponnaluri, inventor Francis Barany, Ph.D., and applicants' undersigned attorney is gratefully acknowledged. The substance of the interview is summarized below.

The rejection of claims 120-125, 128, 136-137, and 148 under 35 U.S.C. § 112 (1st para.) for failure to satisfy the written description requirement is respectfully traversed in view of the above amendments. Support for the binding to "complementary nucleic acids at uniform hybridization conditions" is found on page 49, lines 15-18. Support for the "differs in sequence from its adjacent capture oligonucleotide probe, when aligned to each other by at least 25% of the nucleotides" limitation is found in original claim 81 ("each capture oligonucleotide differs from its adjacent capture oligonucleotide on the array by at least 25% of the nucleotides") and page 42, lines 6-34 of the specification (showing capture probe sequences that are aligned to indicate where there is identity and a lack of identity).

The rejection of claims 120-125, 128, and 136-137 under 35 U.S.C. § 112 (2nd para.) for indefiniteness is respectfully traversed in view of the above amendments.

The rejection of claims 120-125 and 136-137 under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 5,744,305 to Fodor et. al., ("Fodor") is respectfully traversed.

Fodor relates to the preparation of arrays of polymeric materials attached to a solid support using solid-phase chemistry, photolabile protecting groups, and photolithography. The polymeric materials can be assembled from any of the following monomers: L-amino acids, D-amino acids, synthetic amino acids, nucleotides, pentoses, and hexoses. Fodor does not show "capture oligonucleotide probes each having greater than sixteen nucleotides and being designed to bind to complementary nucleic acids at uniform hybridization conditions, wherein each capture oligonucleotide probe of the array differs in sequence from its adjacent capture oligonucleotide probe, when aligned to each other by at least 25% of the nucleotides". Indeed, Figures 1, 2, 6, 7, and 8 of Fodor do not even show oligonucleotide probes with greater than 16 nucleotides, and the adjacent capture oligonucleotide probes are nearly identical. The reason for this is that the array of Fodor is predicated on changing just one base to detect differences.

As pointed out at the personal interview, the above-quoted limitation of the pending claims is important in distinguishing the claimed invention. In particular, the probes in Fodor's array carry the burden of both detecting a target nucleic acid and generating a

signal correlated to detection of the target. Designing a plurality of capture probes to detect and signal detection of a plurality of different nucleic acid targets at one time on a single array (i.e. under uniform hybridization conditions) is a difficult task using Fodor's technology. Moreover, since Fodor's capture probes must accomplish the diverse tasks of detection and signaling, its system is particularly susceptible to producing false signals. By contrast, detection and signaling of such detection can be readily and accurately achieved with the device of the present invention, because the above characteristics of the capture probes. One example of how the device of the present invention achieves such improved results involves its use with ligase detection reaction ("LDR"). As shown, for example, in Figure 3 of the present application, the presence or absence of a particular base in a target nucleic acid sequence is detected by LDR using probes having target specific portions (shown as hatched). One of those probes has capture probe specific portion Z1, Z2, Z3, or Z4 (shown as solid) which does not bind to the target nucleic acid but is important in the subsequent step of array capture. When target nucleic acid is present, the probes are ligated and the sample is contacted with an array so that capture probe-specific portion Z1, Z2, Z3, or Z4 hybridize to its complementary capture probes. When the target nucleic acid is in the sample during LDR (so that the LDR probes ligate), that ligation event will form a product having a marker which can be detected when that product is hybridized a capture probe on the array at capture probe-specific portion Z1, Z2, Z3, or Z4. Use of the present device with an LDR process is only one example of how that device can be utilized. The important thing to remember is that, with the claimed device, detection and signaling can be carried out separately, facilitating the array capture and detection of a plurality of different nucleic acids at one time. Since Fodor fails to teach or suggest the claimed invention, the rejection based on it should be withdrawn.

The rejection of claims 120-124 and 136-137 under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 5,837,832 to Chee et. al., ("Chee") is respectfully traversed.

Chee teaches arrays of nucleic acid probes on biological chips. The outstanding office action states that SEQ ID NOs: 9 and 10 of Chee constitute capture probes in accordance with the present invention. Applicants respectfully disagree. Firstly, Chee does not say that these sequences are adjacent to one another on the array. However, even if they were, they do not satisfy the "capture oligonucleotide probes each having greater than sixteen nucleotides and being designed to bind to complementary nucleic acids at uniform hybridization conditions, wherein each capture oligonucleotide probe of the array differs in sequence from its adjacent capture oligonucleotide probe, when aligned to each other by at least 25% of the nucleotides" limitation of the claims. In particular, the oligonucleotide

probes of SEQ ID NOs: 9 and 10 each actually stand for 4 different nucleotide sequences depending on what X is selected to be. Since each of the 4 SEQ ID NO: 9s and each of the 4 SEQ ID NO: 10s only differ from another by a single base, each of the 4 SEQ ID NO: 9s and each of the 4 SEQ ID NO: 10s differ from one another by less than 25%. Moreover, when properly aligned, as shown below, it is apparent that SEQ ID NOs: 9 and 10 of Chee, which have 15 nucleotides, have 12-13 identical nucleotides and differ by only 2-3 nucleotides:

TTTATAXTAGAAACC	(SEQ ID NO: 9)
TTATAGXAGAAACCA	(SEQ ID NO: 10)

Since X can be A, T, C, or G, SEQ ID NOs: 9 and 10 have only 2 differences if X is G in SEQ ID NO: 9 and X is T in SEQ ID NO: 10. Otherwise, there will be 3 differences between these sequences. In either event, assuming that SEQ ID NOs: 9 and 10 are adjacent to one another (which there is no evidence of), they fail to satisfy the above quoted capture oligonucleotide claim limitation. As a result, Chee's device suffers from the same deficiencies as those described above with respect to Fodor's device. Accordingly, the rejection based on Chee should be withdrawn.

The rejection of claims120-125, 128, and 137-138 under the judicially-created doctrine of obviousness-type double patenting as unpatentable over U.S. Patent Application Serial No. 08/794,851 ("'851 application") is respectfully traversed in view of applicants' submission of the accompanying terminal disclaimer.

In view of all the foregoing, it is submitted that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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Michael L. Goldman
Registration No. 30,727

NIXON PEABODY LLP
Clinton Square, P.O. Box 31051
Rochester, New York 14603-1051
Telephone: (585) 263-1304
Facsimile: (585) 263-1600

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